eCTD Update

21st Annual DIA Conference for Electronic Document Management

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Overview

- Review of guidances
- Numbers please…
- A word on validation
- Back to the future
- The reviewer's desktop

eCTD Guidance

- Providing Regulatory Submissions in Electronic Format - Human Pharmaceutical Product Applications and Related Submissions
  - All submission types
    - NDA, ANDA, BLA, IND, DMF, Annual Reports, Periodic Safety Reports, Advertising and Promotional Labeling
  - Last Published as Final April 2006
- Preferred Format for Submissions

eCTD Specifications

- eCTD Specifications
  - FDA Module 1 Specification
  - FDA Modules 2 to 5 Specification
  - Study Tagging File Specification
- FDA eCTD Table of Contents Headings and Hierarchy
- Documentation Available On-Line

http://www.fda.gov/cder/regulatory/ersr/default.htm

Other Guidances

- Withdrawn traditional eSubmission
  - 1999 – Providing Regulatory Submissions in Electronic Format – NDAs
  - 2002 – Providing Regulatory Submissions in Electronic Format – ANDAs
  - 2003 – Providing Regulatory Submissions in Electronic Format – Annual Reports for NDAs and ANDAs (*draft)*
- eCTD is only recognized format without a waiver

Be on the lookout for

- Updated Specifications from ICH
  - eCTD Version 3.2.1
  - STF Version 2.2
- FDA Validation Criteria
- Beginning discussions on updating Module 1

FDA eCTD Metrics
2006 DIA Annual Meeting

	Applications	Submissions
DMF	14	17
IND	119	1,312
NDA	71	1,194
ANDA	72	236
BLA	18	599
Total	285	3,358

http://www.fda.gov/cder/regulatory/ersr/ectd.htm

FDA eCTD Metrics
2007 DIA EDM

	Applications	Submissions
IND	239	3,488
NDA	153	2,203
ANDA	117	472
BLA	34	1,070
DMF	46	56
FDA Internal	3	3
Totals	596	7,292

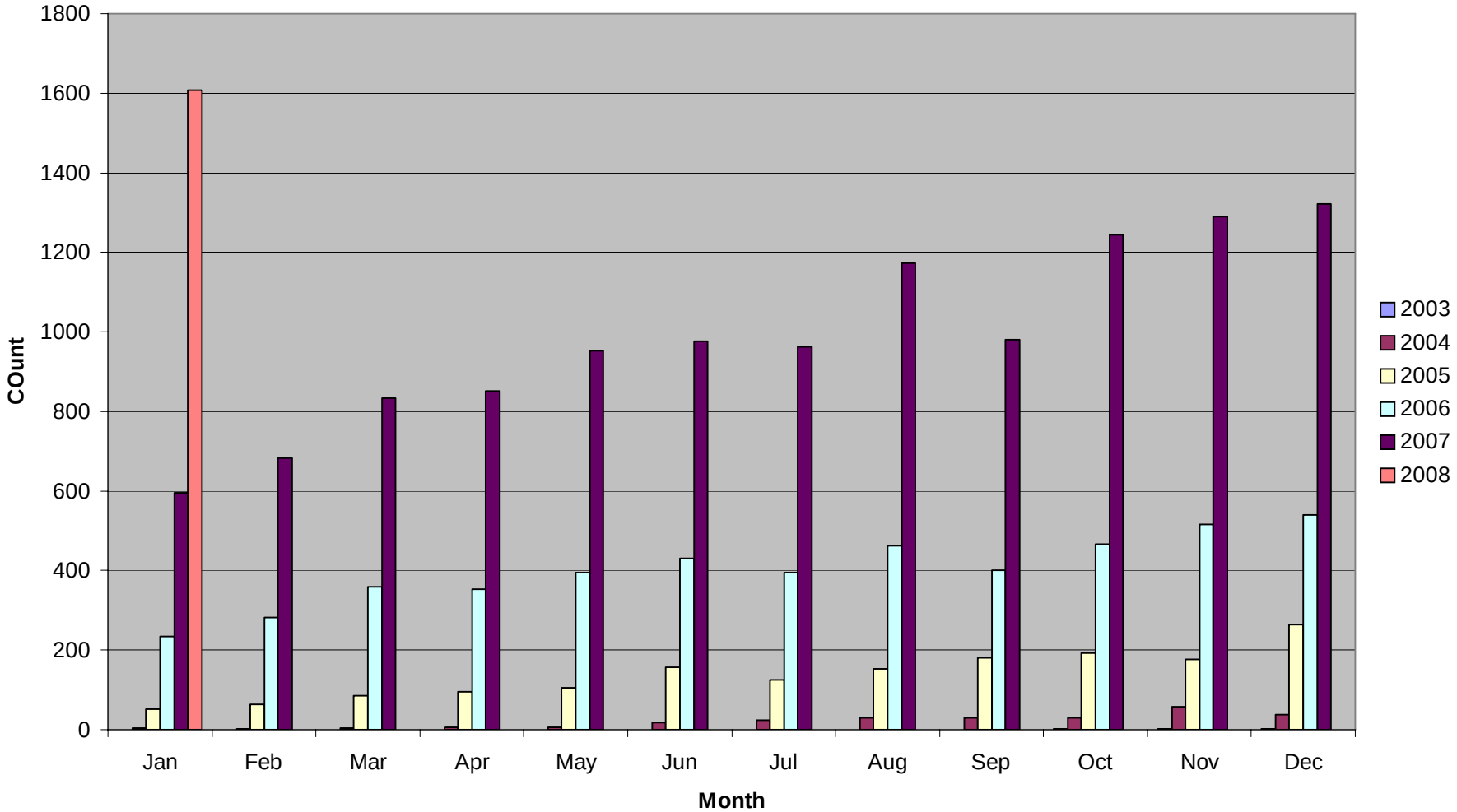
FDA eCTD Metrics
2008 DIA EDM

Application	Count	Submissions
IND	644	10,955
NDA	531	5,184
ANDA	617	1,853
BLA	60	2,221
DMF	135	188
FDA Internal	191	373
Total	2,182	20,773

http://www.fda.gov/cder/regulatory/ersr/ectd.htm

eCTD Submissions

October 2003 - January 2008



eSubmissions – The Larger Perspective

- For 2007
  - Total Submissions 167,490
  - Paper 136,556 (81%)
  - Mixed Paper/Electronic14,025 (8%)
  - Electronic Only 16909 (11%)

A Great Start

Type	Total	Paper		Mixed		Electronic	
NDA Original Initial	124	15	12.10%	70	56.45%	39	31.45%
NDA Original Amendment	13690	9595	70.09%	534	3.90%	3561	26.01%
NDA Efficacy Supplements Initial	159	17	10.69%	62	38.99%	80	50.31%
NDA Efficacy Supplements Amendment	2666	1513	56.75%	127	4.76%	1026	38.48%
NDA Manufacturing Supplements Initial	1987	1211	60.95%	120	6.04%	656	33.01%
NDA Manufacturing Supplements Amendment	1551	1117	72.02%	54	3.48%	380	24.50%
NDA Labeling Supplements Initial	976	84	8.61%	192	19.67%	700	71.72%
NDA Labeling Supplements Amendment	2115	957	45.25%	195	9.22%	963	45.53%
NDA Other Amendment	6903	4187	60.65%	2536	36.74%	180	2.61%

* Numbers reported are draft

http://www.fda.gov/cder/regulatory/ersr/ectd.htm

Progress is Still Needed

Type	Total	Paper	Percentage	Mixed	Percentage	Electronic	Percentage
IND Original	3241	3039	93.77%	82	2.53%	120	3.70%
IND Amendment	84929	77207	90.91%	713	0.84%	7009	8.25%

* Numbers reported are draft

Paper Remains an Issue

eCTD Validation Criteria

- Harmonized between CDER and CBER
- Developing documentation to ensure validation is clear and responses to error documented
- To be published shortly

eCTD Validation Example

Error	Missing file
Severity	Medium
Description	You have referenced a file in the hlink:xref attribute of a leaf and the system is unable to locate the file. It may be missing or you may have mis-spelled the file's name
To Repair	Submit the missing file or correct its name in a later sequence referencing the original leaf using the operation attrribute of "replace"

The FDA's Goal

Implement a standards-based end-to-end fully electronic receipt, review, and dissemination environment

Exchange Standards Organizations

- Development and adoption coordinated with other health-related organizations
  - Accredited, open consensus SDO
    - International Standards Organization (ISO)
    - American National Standards Institute (ANSI)
    - Health Level Seven (HL7)
    - National Council for Prescription Drug Programs (NCPDP)
  - US standards adoption initiatives
    - Consolidate Health Informatics (CHI)
    - Health Information Technology Standards Panel (HITSP)
  - Others
    - Clinical Data Interchange Standards Consortium (CDISC)
    - Global regulatory standards groups (ICH, VICH, GHTF)

HL7 Exchange Standards

- Submission Information
  - Regulated Product Submission Standard
- Product Labeling and Listing Information
  - Structured Product Labeling
- Manufacturing Information
  - Stability Data Standard
- Study Information
  - CDISC HL7 Standards
- Adverse Reaction Reports
  - Individual Case Safety Report Forms
- ECG Information
  - Annotated ECG Waveform Data standard

What Will Standards Mean to Industry?

- Improved harmony across Divisions and Centers
  - Focus is FDA-Wide
- Higher quality submission specifications
  - Formal standards development organizations (SDO), e.g., HL7, ANSI, CEN, have rigorous procedures to ensure the development of quality standards
- Increased ability to influence standards
  - SDOs employ an open process

Enhance FDA Operations

- Increase use of FDA Electronic Submission Gateway
- Leverage metadata accompanying eSubmissions
  - Automate receipt functions
  - Automate validation
  - Automate notification and routing

Enhance Review Capabilities

- Submission Content
  - Janus Study Data Warehouse
  - Integrated Electronic Document Room
- Review Tools
  - WebSDM
  - Patient Profile Viewer
  - iReview/jReview
  - ToxVision
  - GSReview

Enhance Review Capabilities

…Continued

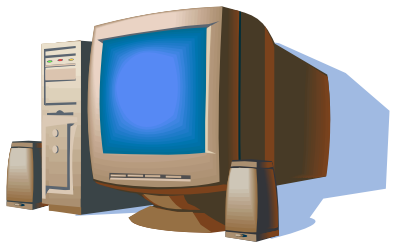
- Improve Decision Support Tools
  - Data Mining
- Standardized Review Templates
  - SMART Template
- Supportive Documentation
  - Electronic Archive of FDA Documentation
  - Enhanced Search Tools
- Review Management Tools
  - Performance Tracking and Analysis
  - Reporting
  - Automated Workflow

Enhance Information Exchange

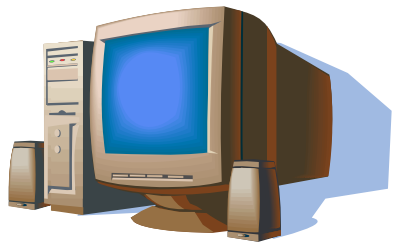
- Capture Investigator Information
  - Firebird
- Two-Way Communications
  - Use FDA ESG to provide two-way communication
  - SPL Collaboration Portal

The Reviewers Desktop

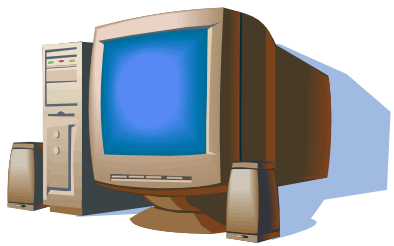
The Previous Situation



Tracking System



EDR (External)



EDR (Internal)

Appl. Type/Number: IND-992265 **Drug Name:** Wonder Drug xyz **Sponsor**
Subm. Type/Number: ANRPT-17 **Current Status/Date:** CREATED-10/19/2(
Supp Doc Number: 542 **Submit Date:** 10/18/2007 **FDA Received Date:**

View Supporting Document

Edit Received Document Set | Edit Assignments | Remove Received Document Set

Unit	UNIVERSAL
Submit Date	10-18-2007
FDA Received Date	10-19-2007
Delivery Method	Gateway

EDR --- You can find this document in the EDR. Clic

Document Properties

Type	Value
No Items Found.	

Document Categories/Subcategories

Category	Subcategory
Original Annual Report	

Linked Communications to this Supporting Document

Primary Author	Function	Checkin Date	State	Final Date	Sent Via	Archive
KENNA, LESLIE A	REV-CLINPHARM-02(Review Noted (NAI))	11/02/2007	Final	11/02/2007	N/A	View
LEE, JONG-HOON	REV-CLINICAL-04(Review Noted (NAI))	01/10/2008	Final	01/10/2008	N/A	View

References

- Electronic Regulatory Submissions and Review website

  http://www.fda.gov/cder/regulatory/ersr/default.htm

- CDER Contact for information on SDTM submissions

  cder-edata@fda.hhs.gov

- Electronic Regulatory Submissions and Review website

  http://www.fda.gov/cder/regulatory/ersr/default.htm

- International Conference on Harmonization

  http://www.ich.org

References

- SPL Information

  www.fda.gov/oc/datacouncil/spl.html

- SPL Contact for information on SDTM submissions

  spl@fda.hhs.gov

- DailyMed

  dailymed.nlm.nih.gov

- SDTM and SEND Information

  www.cdisc.org